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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,855	03/07/2001	Stephen T. Sonis	MT 100 CON	7394

23579 7590 08/06/2003

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	PAPER NUMBER
1614	17

DATE MAILED: 08/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/800,855	SONIS ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-14 and 23-27* is/are pending in the application.

4a) Of the above claim(s) *2, 3, 10, 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,12-14 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Action

Claims 1, 4-6, 12-14, 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schenk et al., supra or Rothwell et al, supra in view of Tilg et al., Transplantation, 56 (1), (1993), 196-201. (of record in parent application 09/065,012).

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rothwell or Schenk in view of Tilg as applied to claims 1, 4-6, 12-14, 23-27 above, and further in view of Stogniew et al., supra.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

The following is responsive to Applicant's amendment received March 12, 2003.

Claims 8, 9 and 15-22 are cancelled. No new claims are added. Claims 1-7, 10-14, 23-27 are currently pending. Claims 2, 3, 10-11 are withdrawn from consideration.

The previous claim rejections under 35 USC 102(b) set forth in paragraphs 1-3 of the office action mailed Feb. 13, 2002 **are withdrawn** in view of Applicant's amendment.

The previous claim rejections under 35 USC 103(a) set forth in paragraphs 6 and 9 of the office action mailed Feb. 13, 2002 **are withdrawn** in view of Applicant's amendment.

The previous provisional rejection under the judicially created doctrine of obviousness-type double patenting set forth in paragraphs 10-12 of the office action mailed Feb. 13, 2002 **are withdrawn** in view of Applicant's amendment.

However, Applicant's arguments traversing the previous claim rejections under 35 USC 103(a) set forth in paragraphs 7-8 of the office action mailed Feb. 13, 2002 have been considered but are, respectfully, not found to be persuasive.

Said rejections are maintained essentially for the reasons given previously in the office action mailed Feb. 13, 2002 with the following additional comment:

It is Applicant's position that the primary references to Schenk et al. and Rothwell et al. as well as the Tilg and Stogniew references fail to disclose or fairly suggest the claimed invention. Specifically, Applicant argues that the Schenk et al. reference discloses the treatment of periodontal disease, not mucositis induced by radiation or chemotherapy as currently claimed. The Rothwell et al. reference discloses treatment of mucositis by administering a combination of tetracycline, hydrocortisone, nystatin and diphenhydramine. However, the claims now require the combination of an NSAID, an inflammatory cytokine inhibitor or a mast cell inhibitor and an MMP inhibitor to treat mucositis induced by radiation or chemotherapy.

Furthermore, neither Tilg nor Stogniew remedy the deficiencies of the Rothwell and Schenk references. Tilg et al. treat patients with pentoxifylline (inflammatory cytokine inhibitor) to decrease TNF-alpha production thereby reducing the side effects associated with bone marrow transplantation. Stogniew discloses administering a radioprotectant, which may additionally include any number of excipients and other actives. None of these references disclose or fairly suggest to one of ordinary skill in the art to use an amount of MMP inhibitor, i.e. tetracycline, minocycline, effective to treat or prevent mucositis. Moreover, there is no suggestion in the prior art of record that one of

ordinary skill in the art combine the MMP inhibitor with an inflammatory cytokine inhibitor to treat mucositis. Based on the teachings of the prior art, one of ordinary skill in the art would not reasonably expect a combination of MMP inhibitor and inflammatory cytokine inhibitor to be effective in treating or preventing mucositis.

Said arguments have been considered but are not found to be persuasive.

The Examiner respectfully submits that the prior art discloses Applicant's claimed invention. Specifically, while Schenk et al. relate to the treatment of periodontal diseases, Schenk specifically discloses the use of topical tetracycline HCl in the treatment of periimplant mucositis. Please see the first three lines of the abstract.

With respect to Applicant's arguments concerning the Rothwell reference, Rothwell teaches an oral rinse composition for treating mucositis comprising tetracycline in addition to other active agents. However, please note that Applicant's claims recite "comprising" language. The term "comprising", "which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the

inclusion of unspecified ingredients even in major amounts"). Please see MPEP 2111.03.

Concerning the Tilg and Stogniew references, the Examiner respectfully submits that Tilg et al. teach that pentoxifylline has been shown to modulate TNF-alpha production thereby reducing the incidence and severity of complications arising from bone marrow transplantation, one of the those complications being mucositis. Please see the abstract, lines 1-4. Stogniew discloses a method of treating or preventing mucositis by administering a radioprotectant composition that may also contain minocycline. (please see col. 8, line 66 to col. 9, line 1 and line 56). Again please note that Applicant's claims recite "comprising" language, which is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997).

Therefore, the Examiner respectfully maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of Schenk or Rothwell to additionally administer an inflammatory cytokine inhibitor such as pentoxifylline because Rothwell, Schenk and Tilg establish that tetracycline and pentoxifylline are known in the art to be useful for treating or preventing mucositis. Modification to combine tetracycline and pentoxifylline, all known to be useful for the same purpose, would have been obvious to one of ordinary skill in the art in view of the fact that the courts have held that "it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose,

in order to form a third composition which is to be used for the very same purpose" Kindly refer to In re Susi, 169 USPQ 423, 426 (CCPA 1971). Furthermore, combination of tetracycline and pentoxifylline into a pharmaceutical composition for treating mucositis would have been motivated by the reasonable expectation that the additive effect of the combination of the tetracycline and pentoxifylline would be successful in treating a subject suffering from mucositis.

Furthermore, the Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of Schenk, Rothwell and Tilg to administer minocycline as the tetracycline compound (as required by claim 7) because Stogniew suggests that minocycline may be useful in the treatment of mucositis and one of ordinary skill in the art would reasonably expect minocycline, which is a tetracycline, to be effective in treating mucositis.

Finally, although Schenk does not disclose the treatment of mucositis induced by chemotherapy or radiation, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Schenk to include treatment of mucositis induced by radiation or chemotherapy because, in view of the disclosures of Rothwell and Stogniew, one of ordinary skill in the art would reasonably expect the topical tetracycline compositions of Stogniew to be equally effective in treating mucositis that is brought on by radiation or chemotherapy.

It is for these reasons that the rejections are maintained.

Claim Objections

Claims 23-26 are objected to because of the following informalities: claims 23-26 are dependent upon cancelled claim 22. Appropriate correction is required.

Conclusion

Claims 1, 4-7, 12-14, 23-27 stand rejected.

Applicant's amendment necessitated the new claim objections presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 703-306-3227. The examiner can normally be reached on Tue-Thur. from 8:30 to 6:00. The examiner can also be reached on alternate Mondays .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725 The fax phone number for the organization where this application or proceeding is assigned is 703-308-7924.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CDM

August 4, 2003

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1200